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武庫川女子大紀要(自然科学)

Crystal Structure of Heterodiquinane Containing a Triazine, an Indoline, and a Pyrrolidine Skeletons Prepared by Photoreaction of 7-Methoxy-3-[1-(methoxyimino) ethyl] -*N*-phenyl-1, 2-dihydro-cinnoline 1, 2-Dicarboximide with Diethyl 1, 3-Acetonedicarboxylate

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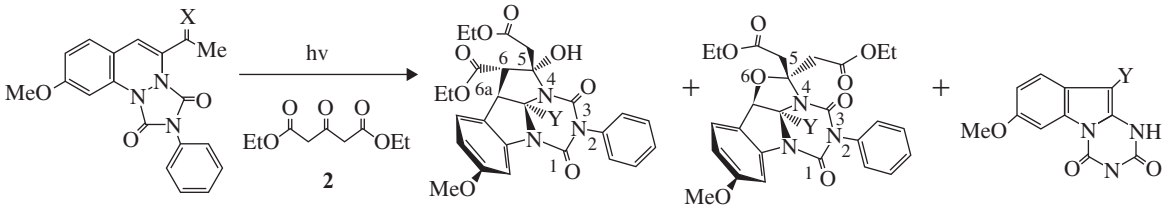
Abstract

The heterodiquinane derivative was prepared from the photochemical reaction of 7-methoxy-3-[1-(methoxyimino) ethyl]-*N*-phenyl-1, 2-dihydrocinnoline 1, 2-dicarboximide with diethyl 1, 3-acetonedicarboxylate in acetonitrile. The structure and the stereochemistry were determined by X-ray diffraction. The compound crystallizes in triclinic, space group $P\bar{1}$ with cell parameters of a = 12.171 (5) Å, b = 12.372 (5) Å, c = 10.431 (2) Å, α = 92.21 (2)°, β = 109.75 (2)°, γ = 89.19 (3)°, and Z = 2 ; the final residual factor is $R1$ = 0.043 for 2489 reflections.

Naturally occurring and artificially synthesized polyquinanes composing of fused five-membered carbocyclic framework have attracted considerable attention from the viewpoints of challenging targets for stereocontrolled syntheses and their biological activities.[1, 2] In the course of our continuous investigations on stereoselective syntheses of heterocyclic angular polyquinane analogues from active urazoles (*N*-phenyl-1, 2-dihydrocinnoline 1, 2-dicarboximide derivatives) **1a** and **1b**,[3-12] we isolated heterodiquinane-based tricycle **3** from the photochemical reaction of urazole **1b** with diethyl 1, 3-acetonedicarboxylate **2** in acetonitrile (Scheme 1). Since the ^{1}H and ^{13}C-NMR analyses did not permit an identification of the framework and the stereochemistry of the compound, the crystal structure was determined by X-ray analysis.

Experimental

General procedure. ^{1}H-NMR (90 MHz) and ^{13}C-NMR (22.5 MHz) spectra were recorded on a Hit-



1a；X=O **1b**；X=NOMe **3** **4** Y；-C(Me)=NOMe **5**

Scheme 1. Reaction scheme.

achi R-1900 spectrometer in a $CDCl_3$ solution with TMS as an internal standard. IR spectra and MS spectra were measured a Shimadzu IR-460 spectrometer and a Shimadzu QP-2000A spectrometer, respectively. 7-Methoxy-3-[1-(methoxyimino) ethyl]-*N*-phenyl-1, 2-dihydrocinnoline 1, 2-dicarboximide **1b** was prepared by the method reported previously.[6, 13] Diethyl 1, 3-acetonedicarboxylate was commercially available and used without further purifications.

Synthesis of heterodiquinane 3. Irradiation of urazole **1b** (0.26 mmol) and an excess of diethyl 1, 3-acetonedicarboxylate **2** (13.0 mmol) in acetonitrile (60 ml) by a 400-W high-pressure mercury lamp through Pyrex filter for 10 h gave a mixture of three products (**3**, **4** and **5**), which were isolated by column chromatography on silica gel, using a mixture of dichoromethane and ethyl acetate as eluent. The photoproduct 5 (3% yield) was already identified as a novel rearranged product in the photochemical reactions of **1b** without nucleophiles.[6] The structure of hetrodiquinane derivative **4** (15% yield) containing a triazinoindoline and an oxazolidine skeletons was confirmed by spectral comparison with the photoproduct of **1b** with **2** in the presence of triethylamine in acetonitrile.[12] The mainly isolated **3** (79% yield) was recrystallized slowly from ethanol to afford compound appropriate for X-ray analysis.

3 ; mp 166-167℃ ; ^{1}H-NMR δ 1.17 (3H, t, Me), 1.36 (3H, t, Me), 1.94 (3H, s, Me), 3.26 and 3.79 (2H, s, CH_2, J=15.4 Hz), 3.83 (3H, s, OMe), 3.94 (3H, s, OMe), 4.08 (2H, q, CH_2), 4.31 (2H, q, CH_2), 5.03 (1H, s, OH), 5.71 (1H, s, 6a-H), 6.61 (1H, dd, Ph), 7.06-7.54 (7H, m, Ph) ; ^{13}C-NMR δ 10.5 (q), 14.0 (q), 14.3 (q), 38.6 (t), 49.9 (d), 55.6 (q), 60.5 (d), 60.9 (t), 61.9 (t), 62.6 (q), 85.3 (s), 91.5 (s), 100.4 (d), 111.2 (d), 121.8 (d), 125.1 (d), 128.4 (d), 128.8 (d), 129.2 (d), 134.7 (s), 142.1 (s), 148.4 (s), 149.7 (s), 154.1 (s), 160.9 (s), 167.9 (s), 170.2 (s) ; MS *m/z* (%) 580 (5, M^+), 416 (100), 227 (32), 187 (30). IR (KBr) 3430, 1738, 1692 cm^{-1}. *Anal*. Found: C, 60.07; H, 5.55; N, 9.77. Calcd for $C_{29}H_{32}N_4O_9$: C, 59.99; H, 5.56; N, 9.65.

X-ray analysis. X-ray analysis of the colorless crystal **3** (size; 0.20 × 0.30 × 0.50 mm) was performed on a Rigaku AFC5R diffractometer with graphite monochromated MoKα radiation (λ = 0.71069 Å). The detailed measurement conditions and crystal data are listed in Table 1. The intensity data were collected at 296 K using the ω-2θ scan technique to a maximum 2θ of value of 55.0°. Of the 7096 reflections which were collected, 6779 were unique (R_{int} = 0.041).

The structure was solved by direct methods with SIR88[14] and expanded using Fourier techniques.[15] The non-hydrogen atoms were refined isotropically. All hydrogen atoms were placed at calculated positions with their isotropic thermal parameters. The final cycle of the full-matrix least squares refinement was based on 2489 observed reflections [I>3.00 σ (I)] and 476 variable parameters. The final R1 and wR2 values were 0.043 and 0.043. The positional parameters are given in Table 2. The selected bond lengths, the bond angles, and torsion angles are shown in Tables 3, 4, and 5. All calculations were carried out with the crystallographic software programe package TEXSAN.[16]

Table 1. Crystal and experimental data

Chemical formula: $C_{29}H_{32}N_4O_9$	
Formula weight = 580.59	
T = 296 K	
Crystal system: triclinic	
Space group: $P\bar{1}$	Z = 2
a = 12.171 (5) Å	α = 92.21 (2)°
b = 12.372 (5) Å	β = 109.75 (2)°
c = 10.431 (2) Å	γ = 89.19 (3)°
V = 1477.2 (9) Å^3	
D_x = 1.305 g/cm^3	
Radiation: MoKα (λ = 0.71069 Å)	
μ (MoKα) = 0.98 cm^{-1}	
F (000) = 612	
Crystal size = 0.20 × 0.30 × 0.50 mm	
Number of reflections measured = 7096	
Number of independent reflections = 6779	
$2\theta_{max}$ = 55.0°	
Number of reflections used = 2489 [I>3.00 σ (I)]	
R indices [I>3.00 σ (I)] : R1 = 0.043, wR 2 = 0.043	
Number of parameters = 476	
Goodness-of-fit on F^2 = 0.96	
$(\triangle / \sigma)_{max}$ = 0.15	
$(\triangle \rho)_{max}$ = 0.14 e-/ Å^3	
$(\triangle \rho)_{min}$ = -0.15 e-/ Å^3	
Measurement: Rigaku AFC5R	
Program system: TEXSAN	
Structure determination: direct method (SIR88)	
Refinement: full-matrix least-squares on F^2	

Table 2. Atomic coordinates and equivalent isotropic displacement (Å^2)

Atom	x	y	z	*B*eq
O(1)	0.0711(2)	0.0803(2)	0.6629(2)	3.83(5)
O(2)	0.3021(2)	0.3665(2)	0.8490(2)	3.95(6)
O(3)	0.6780(2)	0.4724(2)	0.7614(3)	4.68(6)
O(4)	0.3534(2)	0.0553(2)	0.7588(2)	4.57(6)
O(5)	0.3528(2)	−0.1243(2)	0.7506(2)	4.52(6)
O(6)	−0.0693(2)	0.3819(2)	0.3428(3)	4.92(6)
O(7)	0.1247(2)	0.0381(2)	0.3414(2)	3.10(5)
O(8)	0.3417(2)	0.0908(2)	0.2299(3)	5.03(6)
O(9)	0.3654(2)	−0.0576(2)	0.3536(2)	3.84(6)
N(1)	0.2854(2)	0.3119(2)	0.6319(2)	2.69(5)
N(2)	0.1569(2)	0.2461(2)	0.7309(3)	2.83(6)
N(3)	0.1714(2)	0.1551(2)	0.5387(3)	2.59(5)
N(4)	0.0101(2)	0.3007(2)	0.4100(3)	3.56(6)
C(1)	0.5828(3)	0.4146(3)	0.6813(3)	3.24(7)
C(2)	0.5933(3)	0.3704(3)	0.5617(4)	3.91(8)
C(3)	0.5028(3)	0.3098(3)	0.4718(3)	3.62(8)
C(4)	0.4029(3)	0.2938(2)	0.5023(3)	2.87(7)
C(5)	0.3946(3)	0.3392(2)	0.6225(3)	2.69(7)
C(6)	0.4830(3)	0.4014(3)	0.7150(3)	2.90(7)
C(7)	0.2540(3)	0.3137(3)	0.7463(3)	2.81(7)
C(8)	0.1276(3)	0.1537(3)	0.6422(3)	2.77(7)
C(9)	0.2116(3)	0.2559(2)	0.5061(3)	2.57(6)
C(10)	0.2967(3)	0.2259(3)	0.4289(3)	2.66(7)
C(11)	0.3168(3)	0.1036(2)	0.4488(3)	2.56(6)
C(12)	0.2065(3)	0.0594(2)	0.4718(3)	2.61(6)
C(13)	0.1053(3)	0.2579(3)	0.8373(3)	2.90(7)
C(14)	0.1340(3)	0.1886(3)	0.9431(4)	4.34(9)
C(15)	0.0824(4)	0.2052(4)	1.0433(4)	5.5(1)
C(16)	0.0072(4)	0.2878(4)	1.0368(4)	5.8(1)
C(17)	−0.0206(4)	0.3567(4)	0.9312(5)	6.1(1)
C(18)	0.0305(3)	0.3411(3)	0.8311(4)	4.73(10)
C(19)	0.6757(4)	0.5215(4)	0.8856(5)	5.3(1)
C(20)	0.2292(3)	−0.0416(3)	0.5572(3)	2.96(7)
C(21)	0.3178(3)	−0.0280(3)	0.6981(3)	3.29(8)
C(22)	0.4357(4)	−0.1229(4)	0.8906(4)	5.1(1)
C(23)	0.4705(6)	−0.2321(5)	0.9288(6)	8.6(2)
C(24)	0.1137(3)	0.3320(3)	0.4314(3)	2.86(7)
C(25)	0.1469(3)	0.4376(3)	0.3920(5)	5.1(1)
C(26)	−0.1843(4)	0.3413(5)	0.3096(6)	7.3(1)
C(27)	0.3416(3)	0.0472(3)	0.3306(3)	3.18(7)
C(28)	0.3720(3)	−0.1248(3)	0.2379(4)	4.44(9)
C(29)	0.2547(5)	−0.1592(5)	0.1488(6)	8.5(2)

*B*eq = (4/3) $\Sigma_i \Sigma_j \beta_{ij} (\boldsymbol{a}_i . \boldsymbol{a}_j)$

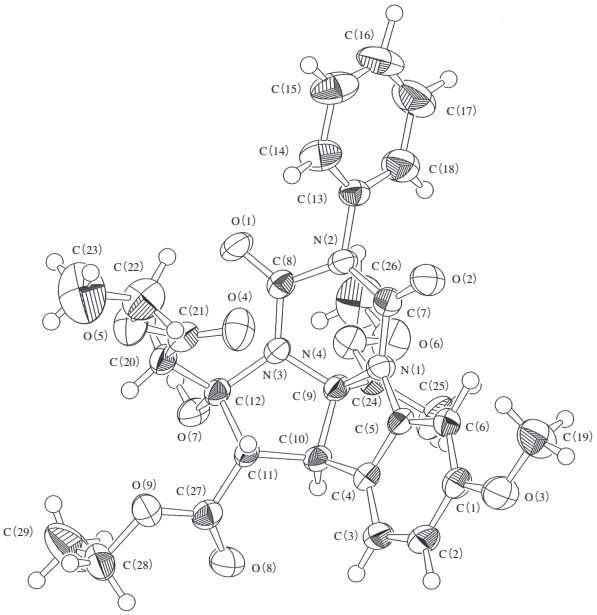


Fig. 1. ORTEP drawing of the title compound (**3**) along with the atomic labeling scheme.

Results and Discussion

An ORTEP drawing of **3** is illustrated in Fig.1 along with the atomic labeling scheme. The compound **3** has an intricate heterodiquinane framework containing a triazine, an indoline, and a pyrrolidine skeletons and these rings are *cis*-fused at axes of N(1)-C(9), N(3)-C(9), and C(9)-C(10). The torsion angles of C(7)-N(1)-C(9)-C(10), N(3)-C(9)-C(10)-C(4), and C(8)-N(3)-C(9)-C(10) are -154.8(3)°, -130.0(2)°, and 158.5(2)°, respectively.

The stereochemistry of the ethoxycarbonylmethyl group at C-5 and the ethoxycarbonyl group at C-6 (Scheme 1) was determined as *endo* and *exo* configurations with respect to the *cis*-fused indoline-pyrrolidine ring on the basis of the ORTEP drawing. Further inspection of the ORTEP figure reveals that the ethoxyl group in the *endo*-position is just above the phenyl ring of indoline. This special arrangement can be also deduced from ^{1}H-NMR data of **3**. The *endo*-ethoxyl protons on the ^{1}H-NMR spectrum resonate at much higher field than *exo*-ethoxyl protons by diamagnetic anisotropy of the phenyl ring (δ 1.17, 4.08 in *endo*-position and δ 1.36, 4.31 in *exo*-position). The space distance between the methylene carbon C(22) of the

Table 3. Selected bond lengths（Å）

Atom	Atom	Distance	Atom	Atom	Distance
O(7)	C(12)	1.405(3)	N(1)	C(5)	1.412(4)
N(1)	C(7)	1.370(4)	N(1)	C(9)	1.470(4)
N(2)	C(7)	1.418(4)	N(2)	C(8)	1.413(4)
N(3)	C(8)	1.356(4)	N(3)	C(9)	1.440(4)
N(3)	C(12)	1.481(4)	C(4)	C(5)	1.388(4)
C(4)	C(10)	1.508(4)	C(9)	C(10)	1.546(4)
C(9)	C(24)	1.520(4)	C(10)	C(11)	1.541(4)
C(11)	C(12)	1.551(4)	C(11)	C(27)	1.509(5)
C(12)	C(20)	1.530(4)	C(20)	C(21)	1.505(4)

Table 4. Selected bond angles（°）

Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
O(7)	C(12)	C(11)	106.1(2)	O(7)	C(12)	C(20)	111.0(2)
N(1)	C(5)	C(4)	109.0(3)	N(1)	C(9)	C(10)	104.1(2)
N(1)	C(9)	C(24)	108.3(2)	N(3)	C(12)	C(11)	100.8(2)
N(3)	C(12)	C(20)	113.6(3)	C(4)	C(10)	C(9)	103.3(2)
C(5)	N(1)	C(7)	127.7(2)	C(5)	C(4)	C(10)	110.5(3)
C(8)	N(3)	C(9)	119.1(3)	C(8)	N(3)	C(12)	126.2(3)
C(9)	N(3)	C(12)	113.4(2)	C(9)	C(10)	C(11)	103.9(2)
C(10)	C(11)	C(12)	106.3(3)	C(10)	C(11)	C(27)	112.2(3)
C(11)	C(12)	C(20)	113.9(3)	C(12)	C(11)	C(27)	112.9(2)

Table 5. Selected torsion angles（°）

Atom	Atom	Atom	Atom	Angle	Atom	Atom	Atom	Atom	Angle
O(1)	C(8)	N(3)	C(9)	165.0(3)	O(1)	C(8)	N(3)	C(12)	−29.0(5)
O(2)	C(7)	N(1)	C(5)	22.1(5)	O(2)	C(7)	N(1)	C(9)	−172.0(3)
O(7)	C(12)	N(3)	C(8)	106.2(3)	O(7)	C(12)	N(3)	C(9)	−87.1(3)
O(7)	C(12)	C(11)	C(10)	85.1(3)	O(7)	C(12)	C(11)	C(27)	−38.3(3)
N(1)	C(9)	N(3)	C(8)	46.6(4)	N(1)	C(9)	N(3)	C(12)	−121.1(3)
N(1)	C(9)	C(10)	C(4)	−14.3(3)	N(1)	C(9)	C(10)	C(11)	104.7(3)
N(3)	C(9)	N(1)	C(5)	126.5(3)	N(3)	C(9)	C(10)	C(4)	−130.0(2)
N(3)	C(9)	C(10)	C(11)	−10.9(3)	N(3)	C(12)	C(11)	C(10)	−30.6(3)
N(3)	C(12)	C(11)	C(27)	−154.0(2)	C(7)	N(1)	C(9)	C(10)	−154.8(3)
C(8)	N(3)	C(9)	C(10)	158.5(2)	C(8)	N(3)	C(9)	C(24)	−74.8(3)
C(8)	N(3)	C(12)	C(11)	−141.8(3)	C(9)	N(3)	C(12)	C(11)	24.9(3)
C(9)	C(10)	C(11)	C(12)	26.1(3)	C(10)	C(9)	N(3)	C(12)	−9.3(3)

endo-ethoxyl group and least-squares plane of the phenyl ring having the methoxyl group is 6.050 Å.

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要　約

7−メトキシ−3−[1−(メトキシイミノ)エチル]−N−フェニル−1, 2−ジヒドロシンノリン 1, 2−ジカルボキシイミドと 1, 3−アセトンジカルボン酸ジエチルをアセトニトリル溶媒中で光反応を行い、表題のヘテロジキナン誘導体を得、X 線回折によりその構造と立体化学を決定した。その化合物は三斜晶系、空間群 $P\bar{1}$、格子定数 a = 12.171 (5) Å, b = 12.372 (5) Å, c = 10.431 (2) Å, α = 92.21 (2)°, β = 109.75 (2)°, γ = 89.19 (3)°, 単位胞内の分子数 Z = 2 で、2489 の反射数に対し R 因子は 0.043 であった。